

CHANGING CONCEPTS IN THE TREATMENT OF PITUITARY ADENOMAS*

The Charles A. Elsberg Lecture

JAMES L. POPPEN

Department of Neurosurgery, Lahey Clinic, Boston

MR. PRESIDENT and Members: It is indeed an honor to appear as the Charles A. Elsberg lecturer tonight, as I realize the qualifications of the neurosurgeons who have preceded me.

I met Dr. Elsberg on only one occasion, at the twilight of his illustrious neurosurgical career. I shall always remember that meeting. After an informal introduction to him, I told him that I had learned much from his monumental work on spinal cord lesions, and I was very sorry not to have had the opportunity to see him operate. At the time, we were standing in one of the surgical amphitheaters at the Neurological Institute. One of the then-younger neurosurgeons was in the process of exposing a posterior fossa tumor. Dr. Elsberg immediately exclaimed, "I shall change my clothes and enter *this* operation!"—which he promptly did. So I at least had the privilege of actually seeing him perform a portion of an operation, probably one of his last.

There is no question that Dr. Elsberg's name will be remembered as long as there is a need for neurosurgeons to operate on surgical spinal cord lesions, because of his memorable, comprehensive monograph on this subject. Those of you who had the opportunity to work with him while he was active are fortunate. I feel that I, and those of us who did not have the privilege of working with him, have learned much from his writings.

It is my purpose tonight to discuss the problems related to pituitary adenomas—namely, the chromophobe and chromophil tumors.

For many years, particularly in the past two decades, the decision

* Presented at the meeting of the New York Society of Neurosurgery, held at The New York Academy of Medicine, May 15, 1962.

as to whether patients with pituitary adenomas should be subjected to surgical intervention immediately or given an initial trial of radiation has been most difficult.

A great difference of opinion has existed between radiologists and neurosurgeons; these opinions persist among various members of the neurosurgical profession. The status of the patient's vision is almost the sole consideration, except for certain acromegalics who have progressive body changes and often serious headaches.

Obviously, surgery is indicated before a trial of radiation is given for patients who have seriously affected vision, or for those who show evidence of a sudden hemorrhage into a pituitary adenoma (pituitary apoplexy). Likewise, there are many patients who show only a slight visual field defect, for whom all of us agree that radiation should be tried before operation is considered.

On the other hand, there is a large group in which failure of vision has progressed to a moderately severe degree, so that the decision as to the type of therapy causes great concern. We must, of course, be aware that when complete bitemporal hemianopsia has taken place, patients may be seriously handicapped even though the visual acuity is normal. The opposite may also occur—the visual acuity may be greatly diminished with no demonstrable field defect. Increased intracranial pressure from internal hydrocephalus may be caused either by extension of an adenoma into the third ventricle or by posterior extension, compressing the pons and, indirectly, the aqueduct of Sylvius.

In order to clarify our thinking, as well as to reinforce our previous judgment as to the proper course of treatment for a patient who has a pituitary adenoma, it seemed worthwhile to review thoroughly the histories of all patients who have been studied and treated in our neurosurgical unit at the Lahey Clinic since 1932. The final follow-up has been rewarding, particularly so since several of the patients have had follow-up studies well over 35 years—they were followed initially by Dr. Cushing, then by Dr. Horrax and, finally, by me.

I shall begin with a brief historical background. It will be recalled that the only known treatment for pituitary adenomas in the earliest years of their recognition was surgical removal of such portion of the adenoma as was possible. Sir Victor Horsley,¹ in a paper published in 1906, mentioned that he had operated on a patient with pituitary adenoma by a frontal approach, but that he did not like it. He suggested

that the temporal approach be utilized because the patient in whom he had used the frontal approach suffered considerable softening of the frontal lobe as a result of ligation of veins entering the sagittal sinus, which would not have occurred if the temporal route had been used.

X-ray treatment was instituted by Gramegna² in an acromegalic patient in 1909, and then was used only occasionally until 1920, when Sosman and others felt that x-ray irradiation was of merit in certain cases of pituitary tumors. Dandy,³ however, stated that recourse to radium or x-ray treatment had, in his experience, been entirely futile.

Krause,⁴ in 1905, suggested the frontal approach more or less like that used today. Schloffer,⁵ in 1906, introduced the transsphenoidal approach which was greatly modified by Hirsch⁶ in 1909.

Certainly, neurosurgeons have felt that more lasting results could be obtained by an intracranial operation, even though the initial operative mortality was higher than with the transsphenoidal operation as devised by Hirsch. I feel that the statistics shown by Hirsch justify his operation for the treatment of pituitary adenomas, particularly for adenomas that have eroded into the sphenoid sinuses with no suprasellar or extrasellar extensions.

The utilization of cortisone derivatives has been invaluable in reducing the operative risk in the uncomplicated cases, and particularly in the large parasellar extensions, to well below 5 per cent. Ray⁷ recently reported that no deaths occurred postoperatively in 80 patients subjected to 85 operations.

Irradiation in the treatment of pituitary adenomas was employed largely as an adjunct to surgery after partial removal of the pituitary adenomas until the middle 1930's. After this, radiation was utilized before and after surgery in the treatment of these lesions. In general, a trial of radiation was advocated for patients whose vision was only slightly to moderately affected, but because of the high percentage of patients so treated who eventually had to be subjected to surgery, most neurosurgeons became discouraged and doubted that this was a lasting form of treatment. Furthermore, in some instances vision continued to fail during x-ray treatment to a point at which it was doubtful whether it could be restored by surgery.

In spite of the reports by Sosman⁸ in 1939 and by Davidoff and Feiring⁹ in 1948, which indicated that in about 50 per cent of patients with chromophobe adenomas vision was benefited by radiation, this

did not appear to be the consensus. Certainly, the experiences of others (Frazier,¹⁰ 1930; Cairns,¹¹ 1935; Rand and Taylor,¹² 1935) were far from encouraging.

Up to 1950, our position concerning the efficacy of radiation in the treatment of pituitary adenomas was that it should be given a trial before employing surgical intervention when vision was only slightly or moderately affected. Patients undergoing such treatment had careful follow-up study, and their visual acuity and visual fields were checked at frequent intervals. If they did not improve or if the vision was not held at a useful level after treatment, they were subjected to operation.

During the period from 1932 to 1949 inclusive, we utilized the standard 200 kv. apparatus and delivered a total dose of from 800 to 2,500 roentgens to the tumor, the tumor dose in any one series being 800 to 900 r. We were far from satisfied with the results of this type of irradiation during this period and our own impression was that a large percentage of patients so treated eventually had to be operated on. This impression, as will be seen, has been borne out by subsequent investigations.

Beginning with the year 1950, Dr. Trump at M.I.T., and our radiologists, starting with Dr. Hare and continuing later with Dr. Smedal and associates, have utilized the 2-million volt x-ray apparatus for treatment of pituitary adenomas, using the rotational method and delivering 4,000 r to the tumor by daily treatments for a period of about 20 days. Without question, there are other forms of treatment by the use of destructive radiation to the pituitary body; however, our experience with high voltage therapy has been solely with the 2-million volt apparatus.

From the very start of the use of this type of therapy, we became aware of the fact that nearly all the patients so treated responded most favorably and only a few came to operation. This fact had previously been reported by Horrax^{13, 14} and others of our group at the Lahey Clinic. The patients in the group that I am reporting were disabled to a marked degree because of diminished vision, intractable headache, apoplexy, and a few showed beginning physical changes, such as those seen in acromegaly. In a few of the acromegalic patients the sella turcica was only moderately enlarged if at all; in all the others the sella turcica was greatly changed from the normal. Encephalograms and arteriograms were used before surgery was instituted in the more recent patients,

because, in a few instances, large intracranial aneurysms simulating pituitary adenomas were disclosed at the time of operation.

To clarify our findings in the two major groups of pituitary adenomas, it seems best to condense the information into table form, followed by pertinent comment.

TABLE I.—PITUITARY ADENOMA—360 PATIENTS

	SEX	
	<i>Chromophobe (290 patients)</i> Patients	<i>Chromophil (70 patients)</i> Patients
Male	145 (50%)	28 (40%)
Female	145 (50%)	42 (60%)

It seems clear that the incidence of pituitary adenomas in 360 patients, of whom 290 proved to have chromophobe pituitary adenomas, is equal in males and females, with the possible exception of the chromophil adenomas. The latter tumor appeared to favor the female.

TABLE II.—PITUITARY ADENOMA—360 PATIENTS

<i>Years</i>	AGE	
	<i>Chromophobe</i> <i>Per cent</i>	<i>Chromophil</i> <i>Per cent</i>
1-19	2	6
20-29	11	21
30-39	16	33
40-49	29	26
50-59	28	10
60 and over	14	4

Pituitary adenomas of both groups occur most frequently in the middle decades, with the possible exception that chromophil adenomas occur less frequently after the age of 50 years.

TABLE III.—PITUITARY ADENOMA—360 PATIENTS—
SUBJECTIVE SYMPTOMS

	<i>Chromophobe (290 patients)</i> Patients	<i>Chromophil (70 patients)</i> Patients
Headaches	246 (85%)	64 (91%)
Visual changes	255 (88%)	46 (66%)
Weight changes (increase)	149 (51%)	44 (62%)
Skin and hair changes	194 (67%)	30 (43%)

Headaches and skeletal changes were the major complaints of patients with chromophil adenomas, whereas the visual change was the major initial complaint of patients with chromophobe pituitary adenomas. Smooth, silky skin with a loss of, or greatly diminished hair in the axillary and pubic regions was most frequently found in the chromophobe patients, whereas coarse, oily skin and increased hair were the rule in the chromophil patients.

TABLE IV.—PITUITARY ADENOMA—360 PATIENTS—
SUBJECTIVE SYMPTOMS (cont'd)

	<i>Chromophobe (290 patients)</i> Patients	<i>Chromophil (70 patients)</i> Patients
Loss of libido	175 (60%)	28 (40%)
Amenorrhea	109 (81% of females)	32 (76% of females)
Testicular atrophy	96 (33% of males)	23 (82% of males)

Loss of sexual drive was the chief complaint in the majority of patients with chromophobe adenomas, whereas this is much less true in patients in the early stages of acromegaly, at which time libido might be temporarily increased. Amenorrhea occurred in the majority of women in both groups. Testicular atrophy was frequently noted in male patients, however, dependent entirely on the stage to which the hypopituitarism had advanced. It was found in only a few of the patients early in the course of their disease.

TABLE V.—PITUITARY ADENOMA—BLOOD PRESSURE CHANGES

	<i>Chromophobe</i>	<i>Chromophil</i>
Normal	47%	43%
Below normal	16%	17%
Above normal	37%	40%

Blood pressure changes seemed to occur with equal frequency in the two groups.

TABLE VI.—PITUITARY ADENOMA—ANEMIA

<i>Chromophobe</i>	<i>Chromophil</i>
10%	4.2%

Anemia occurred about twice as frequently in the chromophobe group as in the chromophil group.

TABLE VII.—PITUITARY ADENOMA—VISUAL CHANGES

	<i>Chromophobe (290 patients)</i> Patients	<i>Chromophil (70 patients)</i> Patients
Visual changes	255 (88%)	46 (66%)
Visual acuity bilateral	232 (80%)	39 (56%)
Visual acuity unilateral	23 (8%)	7 (10%)
Optic pallor	228 (79%)	30 (43%)

Visual changes were present in most of the patients who had chromophobe pituitary adenomas. It must be remembered that visual field changes may occur without diminished acuity; and likewise, diminished acuity may take place without visual field changes. Also, cranial nerve involvement may be present without visual acuity or visual field change.

TABLE VIII.—PITUITARY ADENOMA—VISUAL FIELDS—360 PATIENTS

<i>Chromophobe (290 patients)</i>	<i>Chromophil (70 patients)</i>
246 (85%)	42 (60%)

TABLE IX.—PITUITARY ADENOMA—VISUAL FIELDS—360 PATIENTS (cont'd)

	<i>Chromophobe (290 patients)</i> Patients	<i>Chromophil (70 patients)</i> Patients
Bitemporal hemianopsia	208 (72%)	35 (50%)
Unilateral field defect	22 (7.5%)	5 (7%)
Homonymous hemianopsia	14 (5%)	
Bilateral nasal defect	1 (0.3%)	
Unilateral nasal defect	1 (0.3%)	2 (1%)

Tables VIII and IX demonstrate the occurrence and types of visual field changes. It is important to test the visual fields on the tangent screen, not only with the large target but also with the 1 mm. target. In many instances, the latter will demonstrate a field defect without the patient actually being aware that a defect is present.

TABLE X.—PITUITARY ADENOMA—X-RAYS

	<i>Chromophobe (290 patients)</i> Patients	<i>Chromophil (70 patients)</i> Patients
Uniform balloon sella	281 (97%)	68 (97%)
Unilateral sella defect	9 (3%)	2 (3%)

In the majority of patients a greatly enlarged, uniformly ballooned sella, with either complete erosion of the posterior clinoids or undercutting of the anterior clinoids, was noted in the majority of patients with chromophobe adenomas as well as in those with chromophil adenomas. A unilateral sellar defect was seen infrequently in our group of patients, even though a slight unilateral disparity was not unusual.

TABLE XI.—PITUITARY ADENOMA—CRANIAL NERVE PARALYSIS

	<i>Chromophobe (290 patients)</i> Patients	<i>Chromophil (70 patients)</i> Patients
3rd nerve—oculomotor	14 (4.8%)
6th nerve—abducens	9 (3%)	1 (1.5%)
5th nerve—trigeminal	3 (1%)
3rd and 5th nerves	2 (0.6%)

Third cranial nerve paralysis was the most common cranial nerve involvement in our patients. Many of the histories, as well as findings in these cases, were suggestive of ruptured intracranial aneurysm, but proved to be the result of either pituitary apoplexy or marked unilateral parasellar extension.

TABLE XII.—PITUITARY ADENOMA—APOPLEXY AND HEMORRHAGIC NECROSIS

	<i>Chromophobe (290 patients)</i> Patients	<i>Chromophil (70 patients)</i> Patients
	30 (about 10%)	8 (about 11%)
Initial symptom	6 (2%)	2 (3%)
Before irradiation	1 (0.3%)
After irradiation	1 (0.3%)	1 (1.4%)
Before surgery	22 (7.5%)	4 (5.8%)
After surgery	—	1 (1.4%)

Apoplexy and hemorrhagic necrosis occurred in only a few as initial findings. Certainly irradiation was not a factor. Most of the patients who came to surgery with hemorrhage or necrosis had advanced visual changes or other symptoms. Both groups were equally affected.

TABLE XIII.—PITUITARY ADENOMA—DIABETES MELLITUS

<i>Chromophobe (290 patients)</i>	<i>Chromophil (70 patients)</i>
1.3%	6.7%

As was suspected, diabetes mellitus occurred frequently in the acromegalic patients, but also was present in patients with chromophobe adenomas.

TABLE XIV.—PITUITARY ADENOMA—CONVULSIONS

	<i>Chromophobe (290 patients)</i> Patients	<i>Chromophil (70 patients)</i> Patients
Before surgery	5 (1.7%)
After surgery	16 (5.5%)	2 (2.8%)
Before irradiation	9 (3.0%)	2 (2.8%)
After irradiation	1 (0.3%)	1 (1.4%)

Convulsions were noted regardless of whether or not treatment had been instituted, and occurred much more frequently after surgical intervention.

TABLE XV.—PITUITARY ADENOMA—RHINORRHEA—6 PATIENTS

	<i>Chromophobe (290 patients)</i> Patients	<i>Chromophil (70 patients)</i> Patients
Before irradiation	0	0
After irradiation	2	0
Before surgery	0	1
After surgery	3	0

Rhinorrhea occurred with equal frequency after irradiation and surgery.

TABLE XVI.—PITUITARY ADENOMA—TYPE OF TREATMENT

	<i>Chromophobe (290 patients)</i> Patients	<i>Chromophil (70 patients)</i> Patients
200 kv. only (800-2600 r)	55 (19%)	30 (43%)
200 kv. + high voltage	8 (3%)	2 (3%)
High voltage only	73 (25%)	17 (24%)
Surgery only	55 (19%)	1 (1%)
X-ray followed by surgery	47 (16%)	11 (16%)
Surgery followed by x-ray	37 (13%)	5 (7%)
X-ray between surgery	7 (2%)	0
Surgery between x-ray	8 (3%)	4 (6%)

Certainly, in 85 patients the tumor dosage of x-rays was low by our present standards. Since 1950, patients have been given 4,000 roent-

gens by the rotational high voltage apparatus. Various combinations of treatment were instituted: 200 kv. plus high voltage; high voltage only; surgery only; x-ray followed by surgery; surgery followed by x-ray; surgery, x-ray, followed by surgery; x-ray followed by surgery followed by x-ray therapy.

TABLE XVII.—PITUITARY ADENOMA—TYPE OF TREATMENT

Multile surgery	26	
Two operative procedures	21	
Surgery only		8
Surgery with x-ray between		7
Surgery + x-ray		3
X-ray + surgery		3
Three operative procedures	4	
Surgery only		2
Surgery with x-ray between		2
Four operative procedures	1	
Surgery with x-ray between		1

It can be readily seen that even though surgery was instituted, it did not always help the patient. Twenty-six patients were subjected to multiple surgical procedures sandwiched between courses of x-ray therapy, or x-ray therapy was given in the intervals between the numerous surgical procedures. As may be noted, four patients had three, and one patient had four operative procedures, with a number of years intervening between operations.

TABLE XVIII.—PITUITARY ADENOMA—RESULT OF X-RAY THERAPY

	<i>Chromophobe (264 patients)</i>	<i>Chromophil (64 patients)</i>
No headaches	193 78%	51 80%
Visual acuity	<i>Chromophobe (233 patients)</i>	<i>Chromophil (69 patients)</i>
Normal	117 50%	47 68%
Marked improvement	65 28%	9 13%
No improvement	25 11%	6 9%
Deteriorated	26 11%	7 10%

Neither surgery nor x-ray treatment restores the visual acuity to normal in all patients; however, 78 per cent were classified as markedly improved to normal—about 20 per cent showed no improvement to deterioration.

TABLE XIX.—PITUITARY ADENOMA—RESULTS OF X-RAY THERAPY—
200 KV., 110 PATIENTS

	Patients		
200 kv. only	55	50%	Improved
200 kv., came to surgery	38	35%	"
200 kv., came to high voltage	17	15%	"
Improved with high voltage	8		
Improved with high voltage after surgery	5		
Did not improve with high voltage and needed surgery	4		

All types of x-ray therapy, both the 200 kv. and the high voltage, are included in the above table. Headaches, in most instances, were greatly benefited. The results in 110 patients who had x-ray therapy, using 200 kv., were as follows: 50 per cent were improved, 35 per cent required surgery, and 15 per cent came to high voltage therapy. Improvement was noted in eight of the 17 patients who required high voltage therapy. Of the patients who came to surgery after 200 kv., and in whom improvement was only temporary, five were helped by high voltage therapy. Four of the 17 patients were not benefited and needed surgical treatment.

TABLE XX.—PITUITARY ADENOMA—RESULTS OF X-RAY THERAPY
High Voltage, 119 Patients

	Patients		
High voltage only	73		
200 kv. and high voltage	8		
High voltage after other therapy	19		
After surgery	10		
Surgery + 200 kv.	4		
200 kv. + surgery	5		
Improved; no further treatment necessary	100	84%	
High voltage and came to surgery	19	16%	

Of 119 patients who had high voltage therapy, it was the only treatment in 73. High voltage therapy was used after surgery in ten patients; after surgery and 200 kv. in four patients; and after 200 kv. plus surgery in five patients. Eighty-four per cent improved with no further treatment; 16 per cent finally came to surgery.

TABLE XXI.—PITUITARY ADENOMA—VISUAL FIELDS AFTER HIGH VOLTAGE

	<i>Improvement Per cent</i>	<i>Deterioration Per cent</i>
2 weeks	20	2
1 month	43	4
2 months	60	6
3 months	68	7
6 months	78	8
1 year	86	9
2 years	90	10

The greatest improvement occurred within eight weeks after institution of x-ray treatment. The course of treatment is usually divided into 20 treatments, depending on the patient's tolerance. Forty-three per cent of our patients were greatly improved after one month; whereas in many of the remaining patients, improvement did not take place for several months up to two years. In one patient, even though the visual acuity improved within six months, the visual fields did not improve until seven years had elapsed, when they became normal.

Visual acuity and fields should be checked at frequent intervals during the course of treatment. Most patients become astute observers and test their own fields of vision and acuity effectively, even though by rather crude methods. The vision may worsen after the second or third treatment, but soon what was lost is regained. In a few instances the treatments have been interrupted for two or three days. Mild nausea may occur; an increase in headaches may also be noted after the second or third treatment.

If x-ray treatments are to be carried out on a patient whose visual acuity is in a precarious state, the patient should be hospitalized during the initial period of the treatments so that daily records of vision can be made; if vision deteriorates, immediate operation may be carried out.

TABLE XXII.—PITUITARY ADENOMA—REASONS FOR SURGERY FOLLOWING HIGH VOLTAGE AND 200 KV. THERAPY

Cystic tumor	33.3%
Large, rubbery, solid tumor	26.6%
Parasellar extensions	30.0%
Hemorrhagic necrosis	10.0%
Associated aneurysm	
Other	

It is obvious that cystic adenomas and adenomas that have undergone hemorrhagic necrosis will not respond to x-ray therapy. The large, rubbery, fibrous, solid tumors seem to respond less well to either high voltage or 200 kv. therapy.

TABLE XXIII.—PITUITARY ADENOMA—OPERATIVE PATIENTS—180

<i>Surgical deaths—frontal approach</i>	
23 Patients—12.7% (case mortality)	
4 patients—in coma preoperatively	
2 patients—cerebral edema	
1 patient—coronary occlusion on operating table immediately before operation was begun	
All but 2 patients had large extensions under temporal lobes—	
Posterior fossae extension—2	
Under frontal lobes—third ventricle	
Hemorrhagic necrosis—2	
One operative death since 1952	

Of the 360 patients, 180 were subjected to operations, the majority by the frontal approach, others by the temporal and trans-sphenoidal approaches. Twenty-three patients died, a case mortality of 12.7 per cent. All but two of these patients had large extensions under the temporal or frontal lobes or into the posterior fossa. Only one death has occurred since 1952. This lowered mortality, of course, is the result of the use of cortisone derivatives immediately before and after operation, and agents such as Decadron, Urevert, and others, for the treatment of preoperative and postoperative cerebral edema.

TABLE XXIV.—PITUITARY ADENOMA—CAUSE OF DEATHS

	<i>Chromophobe (290 patients)</i>		<i>Chromophil (70 patients)</i>	
	<i>Number</i>	<i>Per cent</i>	<i>Number</i>	<i>Per cent</i>
Same condition	41	13.8	3	4.2
Other condition	34	11.5	15	21.4
Unknown	8	2.7	2	2.8

In patients who were adequately treated, death was directly related to the pituitary condition in approximately 14 per cent of those with

chromophobe adenomas; in about 12 per cent death was caused by other conditions, and in 2.7 per cent the cause was unknown. Patients with chromophil adenomas died from other conditions, although in many instances death was the result of the chromophil adenoma, since diabetes mellitus occurs in 6.7 per cent of such patients, in contrast to 1.3 per cent in those with chromophobe adenomas.

TABLE XXV.—PITUITARY ADENOMA—REPLACEMENT THERAPY

<i>Chromophobe</i>	<i>Chromophil</i>
34%	21%

Various agents were used for therapy—thyroid drugs, steroids, testosterone, or combinations thereof, as seemed necessary.

TABLE XXVI.—PITUITARY ADENOMA

Re-establishment of Menses	
186 Women—149 with Amenorrhea (Premenopausal)	
Surgery only	0
Surgery plus x-ray therapy	5
X-ray plus surgery	3
X-ray therapy only	22
<i>Pregnancy</i>	
After surgery plus x-ray	1
After x-ray therapy	5

Menses are restored infrequently, but in a higher percentage of patients following x-ray therapy than after surgery. This may be due to the fact that the condition is more advanced in patients subjected to surgery.

As can be seen, pituitary adenomas seem to be favorable tumors, as far as longevity and usefulness are concerned, if proper treatment is instituted—chromophil tumors are, perhaps, slightly less favorable with regard to longevity. At the present time, many of our patients are in the seventh and eighth decades.

COMMENT

There can be no question at the present time that both x-ray therapy and surgery have a definite place in the treatment of pituitary tumors.

TABLE XXVII.—PITUITARY ADENOMA—FOLLOW-UP

<i>Years</i>	<i>Patients</i>	<i>Per cent</i>
Less than 1	16	5
1	17	5
2	14	4
3	25	7
4	10	2.5
5-9	92	26
10-14	61	16
15-19	63	17
20-24	27	7
25-29	14	4
30-40	6	1.5
Over 40	1	—
Unknown	14	4
	360	

I can see very little harm in giving a course of x-ray therapy when the presence of a pituitary adenoma is suspected if the encephalograms and arteriograms seem to corroborate the diagnosis. Specimens taken from the brain tissue surrounding the adenoma after high voltage x-ray treatment have shown no changes from the normal, except in cases of pituitary apoplexy, in which the hemorrhage has extruded through the capsule. No definite radiation changes can be seen after radiation therapy, with 4,000 roentgens delivered to the tumor. There is no permanent epilation, and in most instances, none even temporarily, whereas, with 200 kv., areas of epilation are almost certain to result. Radiation necrosis did occur in a few instances after 200 kv. x-ray therapy; this is unknown with rotational high voltage therapy.

No tumefaction has been noted in our patients. In four patients who had exploratory operations, no adenomatous tissue was found, but there was some thickening of the arachnoid. Freeing of the arachnoid did not change the vision; however, it seemed to help the headaches in two instances.

If there is no improvement in the visual acuity or fields in a patient with moderate to severe changes in vision, operation is advised after one month to six weeks. On the other hand, in the review of this group of patients, it seems that if the vision is not deteriorating, and perhaps has slightly improved, one should withhold surgery and keep the patient under close supervision.

I feel that if surgery is to be performed, one must know whether or not the chiasma is in a prefixed position. This can be determined by arteriography. If the anterior communicating or the anterior cerebral arteries are not elevated in the anteroposterior view, a prefixed chiasma is most likely. In these patients the temporal approach is the logical one.

It is interesting to note that the time element, the interval between x-ray treatment and the surgical procedure, has varied. Most of the operations were performed within the first six months, and only a few in from two to five years.

REFERENCES

1. Horsley, V. On the technique of operations on the central nervous system, *Brit. Med. J.* 2:411-23, 1906.
2. Gramegna, A. Un cas d'acromégalie traité par la radiothérapie, *Rev. Neurol. (Par.)* 17:15-17, 1909.
3. Dandy, W. E. Surgery of the brain. In *Practice of Surgery*, D. Lewis, ed., Hagerstown, Md., W. F. Prior Co., 1932, vol. 12, p. 554.
4. Krause, F. Hirnchirurgie, *Die Deutsche Klinik am Eingange des Zwanzigsten Jahrhunderts in akademischen Vorlesungen* 8:953-1024, 1905.
5. Schloffer, H. a) Erfolgreiche Operation eines Hypophysentumors auf nasalem Wege. *Wien. Klin. Wschr.* 20:621-24 (May 23), 1907. b) Weiterer Bericht über den Fall von operiertem Hypophysentumor. *Ibid.*:1075-78 (Sept. 5), 1907.
6. Hirsch, O. Endonasal method of removal of hypophyseal tumors. With report of two cases. *J.A.M.A.* 55:772-74 (Aug. 27), 1910.
7. Ray, B. S. and Patterson, R. H., Jr. Surgical treatment of pituitary adenomas, *J. Neurosurg.* 19:1-8, 1962.
8. Sosman, M. C. The roentgen therapy of pituitary adenomas, *J.A.M.A.* 113: 1282-85 (Sept. 30), 1939.
9. Davidoff, L. M. and Feiring, E. H. Surgical treatment of tumors of the pituitary body, *Amer. J. Surg.* 75:99-136, 1948.
10. Frazier, C. H. A series of pituitary pictures. Commentaries on the pathologic, clinical and therapeutic aspects, *Arch. Neurol. Psychiat.* 23:656-95, 1930.
11. Cairns, H. Prognosis of pituitary tumours, *Lancet* 2:1310 (Dec. 7); 1363-64 (Dec. 14), 1935.
12. Rand, C. W. and Taylor, R. G. Irradiation in treatment of tumors of pituitary gland, *Arch. Surg. (Chic.)* 30:103-50, 1935.
13. Horrax, G. Chromophobe pituitary adenomas: surgical and radiation treatment, *Surg. Clin. N. Amer.* 31:877-81, 1951.
14. Horrax, G. and others. Present-day treatment of pituitary adenomas. Surgery versus x-ray therapy. *New Engl. J. Med.* 252:524-26 (Mar. 31), 1955.